

20030121031

Reprinted from American College of Surgeons 1985 Surgical Forum Volume XXXVI.

Best Available FEB 14 1988

(12)

ARMED FORCES RADIOBIOLOGY
RESEARCH INSTITUTE
SCIENTIFIC REPORT
SR85-34

AD-A164 185

DTIC FILE COPY

COMPARISON OF THE EFFECTS OF SOLUBLE AND PARTICULATE FORMS OF GLUCAN, AN IMMUNOMODULATOR, ON PROSTAGLANDIN SYNTHESIS BY RAT PERITONEAL MACROPHAGES

Gary J. Bowers, MD, Myra L. Patchen, PhD, Thomas J. MacVittie, PhD, Erwin F. Hirsch, MD, FACS, and Mitchell P. Fink, MD

GLUCAN, AN IMMUNOMODULATOR derived from the yeast *Saccharomyces cerevisiae*, exists in two preparations, particulate (glu-P) and soluble (glu-F). Both preparations enhance host antibacterial and antineoplastic resistance (2). Unlike glu-F, glu-P is associated with granulomatous reactions within the reticuloendothelial system (RES) (3) and endotoxin sensitivity (1). Since some of the adverse effects of glu-P may be mediated by prostaglandins (PGs), we compared the effects of glu-P and glu-F on PG production by rat peritoneal macrophages (PM ϕ s).

MATERIALS AND METHODS

Resident PM ϕ s were incubated (10^6 cells/well) in minimum essential medium (MEM) at 37°C. After two hours, cells were washed, then stimulated for five hours with various concentrations of glu-P or glu-F in MEM (1.0 mL/well). Concentrations of immunoreactive (i) thromboxane (Tx) B₂ (stable metabolite of TxA₂) and i6-keto-PGF_{1 α} (stable metabolite of PGI₂) were measured in culture supernatants by radioimmunoassay. Protein content of the PM ϕ monolayer was determined using Bio-Rad. Prostanoid concentrations per microgram of protein were calculated, and the results were expressed as mean percentage (%) change \pm standard error vs control (ie, no glucan). Differences between the groups were assessed by two-way analysis of variance, with drug and dose as independent sources of variation.

RESULTS

Glucan stimulation did not alter viability of the PM ϕ s (trypan blue exclusion). Glucan P and F stimulated synthesis of PGs. As shown in Table 1, iTxB₂ increased with increasing doses of both drugs, glu-P being the stronger agonist. The concentration of i6-keto-PGF_{1 α} in supernatants

From the Armed Forces Radiobiology Research Institute—Defense Nuclear Agency, Bethesda, MD 20814-5145, Work Unit 00146. The views are those of the authors; no endorsement by the Defense Nuclear Agency has been given nor should be inferred.

DISTRIBUTION STATEMENT A

Approved for public release
Distribution Unlimited

66

86 2 14 106

Best Available Copy

Table 1

PG	Glucan	Glucan dose ($\mu\text{g/mL}$)*				Statistics
		0.1	1.0	50	100	
TxB ₂	F	60 \pm 9	116 \pm 20	337 \pm 28	377 \pm 30	Dose: F _{3,72} = 26.8, P < 0.001
	P	141 \pm 17	212 \pm 5	1,722 \pm 265	2,010 \pm 341	Drug: F _{1,72} = 52.7, P < 0.001
6-keto-PGF _{1α}	F	150 \pm 23	255 \pm 28	412 \pm 69	393 \pm 59	Dose: F _{3,72} = 21.6, P < 0.001
	P	131 \pm 15	181 \pm 12	407 \pm 24	473 \pm 66	Drug: F _{1,72} = 0.02, P < 0.05

*N = 10.

also increased with larger glucan doses, but there was no difference in the effect of the two preparations.

DISCUSSION

Glucan-P, but not glu-F, evokes granuloma formation within the major RES organs, consisting of hypertrophic and hyperplastic macrophages (Møs) (2,3). Cotreatment with indomethacin attenuates glu-P-induced granulomogenesis while not interfering with ingestion of glu-P by Møs (3). These data suggest a role for PGs in the pathogenesis of glu-P-induced granulomas. We showed PG release by glucan-stimulated PMøs depends on the preparation of glucan employed. This observation may help explain why glu-F does not induce granuloma formation.

REFERENCES

1. Cook JA, Halkushka P, Wise W: Modulation of macrophage arachidonic acid metabolism: Potential role in the susceptibility of rats to endotoxic shock. *Circ Shock* 9:605-617, 1982
2. DiLuzio NR, Williams D, McNamee R, et al: Comparative tumor-inhibitory and antibacterial activity of soluble and particulate glucan. *Int J Cancer* 24:773-779, 1979
3. Way CF, Dougherty WJ, Cook JA: Effects of essential fatty acid deficiency and indomethacin on histologic, ultrastructural, and phagocytic responses of hepatic macrophages to glucan. *J Leuk Biol* 37:137-150, 1985

DTIC
ELECTE
FEB 14 1988

B



Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-120	